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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/067,892	02/08/2002	Alison A. McCormick	42256	1133

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EXAMINER	
TUNGATURTHI, PARITHOSH K	
ART UNIT	**PAPER NUMBER**
1643	

DATE MAILED: 02/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/067,892	MCCORMICK ET AL.	
	Examiner	Art Unit	
	Parithosh K. Tungaturthi	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 November 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *51-60* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The applicant has timely traversed the non-final rejection in the reply filed on 11/25/2005, and a response to the arguments is set forth.

2. Claims 1-50 have been cancelled

4. Claims 51 and 52 have been amended and 58-60 have been newly added.

5. Claims 51-60 are under examination.

6. The text of those sections of Title 35 U.S.C. code not included in this office action can be found in a prior office action.

Rejections Withdrawn

7. The rejection of claims 52 and 53 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of the applicants arguments.

Response to Arguments and New Grounds of Rejections

8. The rejection of claims 51-57 and 58-59 under 35 U.S.C. 103(a) as being unpatentable is maintained and further reinstated.

The response filed on 11/25/2005 has been carefully considered, but is deemed not to be persuasive. The response argues that none of the references disclose a transient plant expression vector, its transfection into a plant, that the plant transiently

produces the polypeptide, in addition to producing a polypeptide vaccine (inducing an antiidotypic immune response) in a plant cell (page 7 first paragraph).

In response to the applicants arguments, the applicant is reminded of the teachings of the prior art cited in the previous office action. Hawkins et al teach an scFv that is an idiotypic determinant of an immunoglobulin, and that the administration of the scFv generated a polyclonal antidiotypic antibody response, which was detected by testing the sera of the host by ELISA (enzyme immunoassay) and flow cytometry (FACS analysis) (see pages 20-21 and 7, in particular). Fiedler et al does teach the transient expression of plants for the production of scFv (please see the entire document), utilizing the plasmid within which are contained the necessary regulatory elements. In addition, Fiedler et al teach that antibody molecule fused with a linker (see page 206 column 1, in particular), can be made in high quantities in transgenic plant cells, wherein 4-6% to 3-4% of the total protein found in soluble forms in leaves and seed, respectively, can be recombinantly expressed scFv. Fiedler et al also teach that the scFv is expressed in the cytoplasm (introduction, in particular) wherein the Fv are retained in the lumen of the ER, in addition to teaching that recombinant scFv is functionally active.

In response to the Applicants arguments on page 8, 3rd paragraph, wherein the Applicant argues that Tang does not teach a library of linkers that can vary in size, the applicant is reminded that in addition to the library having the formula $(SNN)_{18}$, Tang discusses that the flexible glycine rich sequence such as $(GGGS)_3$ has been used (see introduction, in particular). Thus, the response argues that the Tang reference stating

that the randomization process of Tang et al is performed differently and would produce a different result from applicant's present linker optimization. The response states that the linker Tang et al is 18 amino aids long, being encoded by $(SNN)_{18}$ and is truly a random linker., wherein claim 55 provide a repeated pattern of degenerate repeated triplet nucleotides with specific nucleotides at certain locations. In response to these arguments instant claim 55 is a linker from a randomized library of linkers that vary in size and sequence and the only requirement in claim 55 is that the trinucleotide does not contain the same nucleotide at all three positions (i.e. TTT). Thus, claim 55 is not limited to any specific nucleotides at certain locations not are they restricted to any particular size and as recited, the linkers for a randomized library of linkers.

In response to the Applicant response on page 7, last paragraph, in regard to the claimed invention must mimic the complex structure of an idiotypic on a B-cell lymphoma and induce an immune response against it, the applicant is reminded of the teachings of Casper et al wherein Casper et al teach the use of an idiotype for the treatment of B-cell lymphoma, wherein the idiotype mimics a surface Ig molecule (see entire document). Casper et al further teach the production of the polypeptide in a cell which was transformed by a nucleotide sequence that encoded the polypeptide, which was able to induce a cell mediated immune response (i.e., Th1) as well as polyclonal antibodies (see page 3701, right column, page 3704, right column and Figure 4). Casper et al also teach a polypeptide (i.e., scFv) that has at least two domains of at least one idiotypic epitope and comprises a VH and a VL domain that are from the B cell surface Ig molecule and said VH and VL domains are linked by a linker that is 16

amino acids in length (see Figure 1). Because the scFv (idiotype) was produced and induced the production of polyclonal antibodies that are reactive with the surface Ig on B cell lymphomas, it is inherent that the linker facilitates secretion and correct folding of the scFv to mimic the native form of the surface Ig (i.e., tumor epitope) expressed on the surface of B cell lymphomas. Casper et al also teach that all mice develop a specific anti-Id immune response after vaccination with scFv (figure 2, scFv(adenovirus data) in particular).

The applicant argues that, none of the references discloses producing a polypeptide vaccine (including an antiidiotypic immune response) in a plant cell. The response also argues that there is no assurance that the scFV forms a "correctly folded protein" as claimed and that all of the references except Tang et al used one fixed linker and that Tang et al is not even concerned with obtaining a "correctly folded protein"

In response to applicant's arguments that the references fail to show certain features of applicant's invention, it is reiterated that Hawkins et al teach a scFv that is an idiotypic determinant (i.e. epitope) of an immunoglobulin expressed on the surface of ab cell lymphoma and the scFv is purified and administration of the scFv generated an anti-idiotypic response, clearly indicating that the scFv was in correctly folded form and mimicked the idiotype of the immunoglobulin expressed on the B cell lymphomas (see pages 19-20, in particular. The applicant is reminded that all that is required is that the prior art set forth the substance of the invention that Casper et al teach a SCFV-GM-CSF idiotype protein that induces an immune response, in fact, a significant and specific anti-Id immune response as shown in Figures 2 and 3, indicating that the SCFV-GM-

CSF is correctly folded, thereby mimicking the idiotype expressed by the natural surface Ig expressed in B-cell lymphomas. See also the text at page 3702, where Casper et al states "All mice developed a specific anti-Id immune response after vaccination". Applicant also argues that claim invention indicates a polypeptide vaccine that induces an idiotypic immune response without a need for adjuvant or other immunostimulatory materials" and the polypeptide taught by Casper contains a well-known material for enhancing the immune response. In response to applicant's argument, Casper et al teach that a scFv (adenovirus), which expressed a scFv (i.e., not fused or conjugated to another polypeptide) identical to the scFv (2A12) of the scFv-GM-CSF fusion, was capable of inducing an immune response as shown in Figures 2 and 3. Thus, the scFv lacking GM-CSF taught by Casper et al is capable of inducing an immune response without the need for adjuvant or other immunostimulatory materials.

The Applicants arguments implies that the scFv produced by the methods cited in the art provide for production that have a different physiology from that claimed and therefore, one may not assume that they will fold and process the polypeptide in the same manner as naturally occurs in human cells. In response applicant has not come forth with any evidence that the claimed polypeptide self-antigen is different from that in the prior art and applicant has not made any comparison between the claimed polypeptide self-antigen and that in the prior art to establish unexpected properties showing that the claimed polypeptide self-antigen is, in fact, different (see MPEP 21 13).

In response to the final arguments presented by the applicant "the present invention used a scFv alone without the use of adjuvants or other immunostimulatory

materials to obtain the claimed desired results", the Applicant is reminded that the claimed invention is a method of producing scFv and not the use of it. Hence, it is concluded that the previously cited prior art in combination renders the claimed invention obvious and hence the rejection of claims 51-57 and 58-59 under 35 U.S.C. 103(a) as being unpatentable is maintained.

In response to claim 58, wherein the claim recites "wherein the polypeptide induces the idiotypic-specific immune response without a seed for an adjuvant or other immunostimulatory material, Casper et al teach that a scFv (adenovirus), which expressed a scFv (i.e., not fused or conjugated to another polypeptide) identical to the scFv (2A12) of the scFv-GM-CSF fusion, was capable of inducing an immune response as shown in Figures 2 and 3. Thus, the scFv lacking GM-CSF taught by Casper et al is capable of inducing an immune response without the need for adjuvant or other immunostimulatory materials and as such meets the requirement of claim. In addition, as the claim reads: the intended use of such recitation "wherein the polypeptide induces the idiotype-specific immune response without a need for an adjuvant or other immunostimulatory material" is given no patentable weight; and hence the teachings of Hawkins et al in regard to the induction of the idiotypic-specific immune response read on the claim 58.

In response to claim 59, wherein the claim recites vector is transiently expressed in cytoplasm, Fiedler et el clearly teaches that antibody molecule fused with a linker (see page 206 column 1, in particular), can be made in high quantities in transgenic

plant cells, wherein 4-6% to 3-4% of the total protein found in soluble forms in leaves and seed (which also in part reads on claim 60), respectively, can be recombinantly expressed scFv. Fiedler et al also teach that the scFv is expressed in the cytoplasm (introduction, in particular) wherein the Fv are retained in the lumen of the ER which reads on claim 59, in addition to teaching that recombinant scFv is functionally active.

9. Claim 60 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 60 is vague and indefinite for reciting "allowing the vector to spread through the plant before recovering the polypeptide", because the exact meaning of the phrase is not clear. The phrase "allowing the vector to spread through the plant" renders the claim and the intended invention confusing. Does the applicant mean that the vector is spread through the plant including the roots, stems, etc., ? Or does the applicant mean the recovering of the polypeptide from the leaves and seeds of the plant? As written, it is impossible for one skilled in the art to determine the metes and bounds of the claim. Accordingly, the claims are indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10. Claim 60 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled

in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. THIS IS A NEW MATTER REJECTION.

The response filed on 11/18/2005 has introduces NEW Matter into the claims. Newly added claim recites "allowing the vector to spread through the plant before recovering the polypeptide". The response did not point out where support for newly added claim 60 could be found in the originally filed disclosure. Although the PTO has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims, when filing an amendment an applicant should show support in the original disclosure for new of amended claims. See MPEP 714.02 and 2163.06.("Applicant should therefore specifically point out the support for any amendments made to the disclosure."). Instant claim 60 now recites limitations which are not clearly disclosed in the specification as filed, and now changes the scope of the instant disclosure as filed. Such limitations recited in the newly added claim 60, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112. Applicant is required to provide sufficient written support for the limitations from the claims in response to this office action.

Conclusion

11. No Claims are allowable.

12. **THIS ACTION IS MADE FINAL**. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Parithosh K. Tungaturthi whose telephone number is 571-272-8789. The examiner can normally be reached on Monday through Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

14. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
Parithosh K. Tungaturthi Ph.D.
(571) 272-8789

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER